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Stowaways in the history of science: The case of simian virus 40 and clinical research on federal prisoners at the US National Institutes of Health, 1960

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ABSTRACT

In 1960, J. Anthony Morris, a molecular biologist at the US National Institutes of Health conducted one of the only non-therapeutic clinical studies of the cancer virus SV40. Morris and his research team aimed to determine whether SV40 was a serious harm to human health, since many scientists at the time suspected that SV40 caused cancer in humans based on evidence from *in vivo* animal studies and experiments with human tissue. Morris found that SV40 had no significant effect but his claim has remained controversial among scientists and policymakers through the present day—both on scientific and ethical grounds. Why did Morris only conduct one clinical study on the cancer-causing potential of SV40 in healthy humans? We use the case to explain how empirical evidence and ethical imperatives are, paradoxically, often dependent on each other and mutually exclusive in clinical research, which leaves answers to scientific and ethical questions unsettled. This paper serves two goals: first, it documents a unique—and uniquely important—study of clinical research on SV40. Second, it introduces the concept of "the stowaway," which is a special type of contaminant that changes the past in the present moment. In the history of science, stowaways are misfortunes that nonetheless afford research that otherwise would have been impossible specifically by creating new pasts. This case (Morris' study) and concept (the stowaway) bring together history of science and philosophy of history for productive dialog.

1. Introduction

This article is about "stowaways" in the history of science. The best way to introduce the concept is by way of an analogy taken from ancient Greek literature. In the epic poem *The Iliad*, Hector set sail for his home port of Troy after a failed diplomatic mission. When he arrived, Hector was shocked to discover that his ships had returned with a stowaway, namely Helen, the wife of the ruler of Sparta who was already Hector's arch enemy. The issue of wife abduction could only make matters worse, so Hector resigned himself to circumstances and prepared his army. War ensued; gift horses burst; a heel was pierced; Troy fell. The stowaway may have been there all along, but the moment Helen was discovered in the wrong place everything changed: politically, ethically, and historically.[1]

The history of biology and medicine is teeming with stowaways—viruses, toxins, receptors, and radioactive elements that scientists knew existed, but that turned up (to their minds and to their dismay) in the wrong place, much like Helen of Troy. In 1960,

[1] As with all metaphors, the use of Helen of Troy as an exemplary stowaway has its limits. For an apt example from the history of science and medicine, see Crosby (1972). This classic text argues that world history is explained in part through the migration of pathogens that travel along with people "in their blood and breath" (31) across formerly isolated geographic areas.

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for example, clinical scientist J. Anthony Morris was shocked to discover that the cell culture he had given to healthy men in a study of a respiratory virus carried a stowaway. It was the virus SV40, which scientists at the time suspected could cause cancer in humans. Morris discovered SV40 in his cell culture in June, but he knew it must have been there all along—having appeared in scientists' natural world before it existed in their social milieus. Like Helen of Troy, the discovery of this stowaway changed everything.

Yet the twist in the story of modern medicine is that stowaways offer more than tragedy alone. Stowaways have enabled research that would have been politically dangerous and ethically impossible according to the standards of the time. Like Hector, Morris resigned himself to the new unfortunate circumstances, and carried out what remains to this day the only clinical research on the *in vivo* carcinogenetic effects of SV40. This landmark research on cancer in man was possible because Morris used as human subjects the people whom he had already inadvertently infected with the virus.

The aims of this paper are twofold. The first is to explain the importance of the concept of "the stowaway" for the historiography of the biological and human sciences. We develop this concept from the work of philosophers of history to offer a new analytic device and show that stowaways are a specific subset of contaminant. Stowaways enable research that would otherwise have been untenable, even disallowed, and they do so specifically by altering historical actors' understanding of their past. By recognizing this distinctive feature of stowaways, it is possible to see how stowaways have enabled uniquely valuable, politically freighted, and paradoxical-sounding research: man-made natural experiments.

The second aim of the paper is to introduce an important but little explored case in the history of science and medicine: the first and only *in vivo* clinical study of the cancer virus SV40. In the summer of 1960, Morris and a team of molecular biologists at the US National Institutes of Health (NIH) carried out one of the few clinical trials ever intentionally conducted on an animal virus that researchers thought at the time might cause cancer, namely simian-virus 40 (SV40). With official blessing from the NIH human-subjects review board, Dr. J. Anthony Morris tested the effects of SV40 in federal prisoners who volunteered for transfer to the NIH Clinical Center in Bethesda, Maryland, to serve as research subjects for the NIH National Institute of Allergy and Infectious Diseases (NIAID).[2] Morris initially exposed the men unintentionally to SV40, which was then called "vacuolating virus." But after Morris understood that he had infected 24 men with SV40 in a study involving nasopharyngeal administration of respiratory syncytial virus (RSV), Morris administered a neutralized RSV preparation so that he could study the effects of SV40 in the same human subjects.[3] In the end, Morris found the short-term effects of SV40 unimpressive but nonetheless important: none of the men tested with the modified preparation developed signs or symptoms of infection.[4]

Published in 1961, this study provided the first and almost the only controlled, clinical evidence to address two questions: first, the scientific question of whether the presence of SV40 in tissue cultures invalidated previous research findings on a range of microbes, and, second, the question of whether human health had been jeopardized in vaccine programs for polio and respiratory illnesses that NIH had regulated and sponsored over the previous decade (see Scheffler this volume).[5] Scientists had done numerous preclinical and epidemiological studies of SV40 and have continued to do so as new tools have become available, such as the biotechnological tool PCR.[6] Yet Morris' study remains one of very few clinical studies of SV40. By implication, his findings continue to fuel political questions about corporate and government culpability in cancers that some claim were caused by federally sponsored or regulated vaccination programs, including the US postwar polio vaccination campaign.

The remainder of the paper proceeds in three parts. In Section 2, we elaborate on two distinctive features of the concept of the stowaway. Then in Section 3, we describe and analyze Morris' experiment, which took place at the NIH Clinical Center (Fig. 1). The Clinical Center was an exceptional research site because its local practices and policies were sanctioned by the US government and shaped subsequent regulation. As a result, the Clinical Center should not be considered a typical site, but a wellspring of research conventions promulgated by force of law and custom to other actors and settings, both domestically and internationally. The Clinical Center's singularity makes it all the more essential to study in order to determine how clinical science was practiced and what activities researchers avoided, neglected, or never imagined in the era of what Jonathan Moreno has called "moderate protectionism."[7] Finally, in Section 4, we close by connecting the concept of the stowaway to scholarship in the philosophy and history of biology and biomedicine.

2. Two defining features of stowaways

We give the term "stowaway" a meaning that is specific to the history and philosophy of science and medicine.[8] We use the term to refer to objects that turn up out of place both in historical actors' settings and in historians' accounts of the past. In doing so, we bring together a long history of neo-nominalisms in science and technology studies that includes Bruno Latour's use of the term "non-human actant" in *Science in Action* (1988) and his more recent conceptualization of "invisibles" (2013). We also draw from the work of Joanna Radin (2013) and others who explore the concept of "latent life" to describe techniques for managing temporality. Stowaways such as SV40 differ from the more general category of "contaminant" because stowaways have two defining features.

[2] We use the term "volunteer" advisedly, and as an actors' category (that of researchers), when describing prisoner-subjects as volunteers. A subcommittee of the Clinical Research Committee, which was part of the NIH Clinical Center's Medical Board, served as its human-subjects review committee before federal regulations were enacted in 1974. For details see Stark (2012) and Thomas (2010).

[3] Morris was the first to recover RSV from a chimpanzee exhibiting a cold-like condition called "coryza" (Morris, Blount, & Savage, 1956). The virus was later identified as responsible for a large proportion of the total number of cases of lower respiratory tract infections (which present as bronchitis in human beings) in the United States. Chanock, Roizman and Myers (1957) and Chanock and Finberg (1957).

[4] However, 22 of the 35 subjects exhibited detectable levels of serum antibodies to SV40 present for approximately one and one-half weeks after the experiment. Albert Sabin also ran an SV40 trial on 12 children to support his conclusion that SV40 contained in the oral polio vaccine did not infect humans. Morris, Johnson, Aulisio, Chanock, and Knight (1961) concluded that SV40 induced only a "low grade" or "subclinical" infection in adults when introduced via the respiratory route.

[5] Cutrone, et al. (2005) and Creager (2002), pp. 141–184.

[6] On the revolutionary rhetoric of the polymerase chain reaction (PCR), see Rabinow (1996).

[7] Moreno (2005).

[8] However, we connect it to recent work on theories of "presence" among scholars in the philosophy of history. An excellent starting point for the discussion of presence is an exchange between Runia (2006) and Ankersmit (2006), as well as an edited volume on the theory (Ghosh & Kleinberg ed. 2013). It is also worth noting that the discursive register of contagion has long been used in American life as a concept for representing social disorder. It was used in early 20th century sociology and medicine to figure ideas, sensations, and behaviors as if they were "as communicable as microbes" (Wald, 2008), p. 88. The discursive register of contamination is similar. Building on anthropologist Mary Douglas' definition of dirt as "matter out of place," scholars have shown that discourses of hygiene, pollution, and purity signify the presence of symbolic systems.

Fig. 1. Exterior view of the Clinical Center NIH circa 1953.
Source: Collection: Images from the History of Medicine; Record UI 101441174.

2.1. Stowaways: entities out of place

When people first agree that an entity with specific attributes (e.g., a virus) exists, then this entity has been brought into being, or "performed." People then take the entity into account, and, as a result, imagine their social and biosocial worlds differently than before the entity came into being.[9] For example, SV40 came into being in the 1950s, when scientists identified and labeled the strain.

It is important to distinguish analytically between an entity's "existence" in the natural world and in the social world because the people who constitute the social world tend to think about the natural world historically. Case in point: researchers believed in 1959 that a viral entity then called "vacuolating virus," soon to be designated SV40, existed in their present-day world and, most importantly, they also believed starting in 1959 that SV40 had always existed in the world, even before they had recognized it. SV40's existence in the natural world, they thought, predated its existence in their conceptual world. As a result, this new understanding simultaneously brought a new virus into being, and a new conception of the past—one in which SV40 always already existed even when people could not see it.[10] We argue that once scientists recognized SV40 as part of their social and natural world circa 1960, they could then figure it as a "stowaway"—which is an entity out of place. The stowaway was a misfortune that nonetheless afforded researchers opportunities that otherwise would have been impossible.

Most scholars tend to study such unexpected appearances as discovery, serendipity, accident, or the gift of a fortuitous environment.[11] They have tended to focus on contaminants (often an actors' category as well as an analytic category) as negative findings rather than auspicious accidents for individuals, collectives, and organizations. Stowaways, in contrast, prompt a different response. They may have been previously known in theory, but when people first glimpse them in an unexpected context the stowaways prompt a productive, retrospective reconfiguration of their social and material contexts. SV40, for example, existed in the world in 1960 as one among at least 40 inactive viruses that had recently been identified in monkey kidney substrate. But SV40 became a stowaway when it appeared in an unexpected place, in our case, in NIH scientists' research materials unrelated to cancer. Scientists, staff, and other historical actors have integrated stowaways, like SV40, into existing personal, technical, administrative, and physical systems that raise new questions for history of science and medicine regarding scientific credit, ontological status, and epistemological credibility of findings borne of misfortune. We develop the analytic of the stowaway to explore the seemingly disastrous finding of a previously identified cancer virus at NIH in mid-twentieth century America, which prompted scientists to conduct otherwise-prohibited clinical studies on federal prisoners.

[9] Tomes (1999).
[10] Roth (2012). For a similar argument and empirical case, see Kirsch (2004: 169).
[11] We owe the latter turn of phrase to Joseph V. Brady, a behavioral scientist who sat on the National Commission for the Protection of Human Subjects of Behavioral and Biomedical Research. See http://sitemaker.umich.edu/substance.abuse.history/oral_history_interviews.

2.2. Stowaways: entities that create new pasts

Stowaways challenge historians of science, medicine, and technology to reconsider how we think about and incorporate the past into our scholarship. As present-day history writers, it goes without saying that in our everyday lives we most likely would take SV40 to have a different status and to possess different attributes than did the historical actors we study.[12] The ontological worlds of our historical actors — the universe of things that existed for them—were of course different enough from our own worlds that historians have had to develop analytic techniques to account for these differences. Likewise, actors' moral universes and ethical horizons differed from our own, and we can recognize that even contemporaries disagreed with each other.[13] In our view it is best to refrain from retrospective judgment or moral condemnation of historical actors who set up channels to undertake research on federal prisoners given the pervasiveness of prisoner research in the 1960s.[14]

An important question for historians is how it can be that once new entities are discovered we (as well as our actors) tend to describe them as having always already existed—at the same time that we produce careful accounts of the very processes through which they were brought into being. When historians' explanations converge with those of historical actors, it can be easy to neglect questions about how actors came to think differently about their own past—that is to say, how historical actors' ideas about their own past started to align more closely with *historians'* ideas about the actors' past. As our case illustrates, the past is constituted anew each time new entities, subjects, and actors come into being.[15] As a result, every time a stowaway appears three moments are reconfigured: that (historical) present moment, the past of that (historical) present, and the historian's version of the past, in which multiple temporalities now appear.

Morris' study shows the importance of this point. Morris' research simultaneously validated the presence of the stowaway (SV40) and validated the use of the only human beings that all actors considered physically and morally legitimate to use in pursuit of SV40: namely, federal prisoners. This population was new to the NIH Clinical Center and had apparently volunteered for transfer to Bethesda to participate in intentional-infection experiments. Neither they nor their investigators knew that SV40 was stowed away in cultures used to study RSV, more conventionally known as the common cold. Once SV40 was detected, however, the prisoners who had participated in the respiratory study became understood as the only human population that could be used to examine SV40's effects in human beings. Using the concept of the stowaway, it is possible to see that these actions do not show that Morris and his colleagues bent ethical rules governing the situation because of extenuating circumstances. Rather their decision to conduct a clinical study on the cancer-causing potential of SV40 show that they envisioned the prisoner research subjects as a newly, biologically constituted population.

3. The case: Morris' SV40 study on prisoners in 1960

3.1. Spring 1960: infecting prisoners

In February of 1960, a team of researchers at NIH's National Institute of Allergy and Infectious Diseases proposed a four-part study on Respiratory Syncytial Virus (RSV)[16] to the Clinical Center's Medical Board. J. Anthony Morris was to lead research for the third part of the study. Morris had a Ph.D. in bacteriology, and joined NIH from the Walter Reed Army Hospital.[17] Earlier in his career he had been among the first to demonstrate that an animal virus could make people sick, too.[18] Morris joined the NIH intramural research program in 1959 at the invitation of Dr. Joseph Smadel, head of the NIH Division of Biological Standards, the unit then charged with regulating vaccine production. Morris worked in the NIAID research ward under direction of virologist Vernon Knight, who had moved from Vanderbilt University to direct NIAID's 50-bed service in the Clinical Center earlier that year. Knight's research aimed to determine minimum infectious doses of common respiratory viruses. As Knight explained, the labs "obtained volunteer prisoners for our studies from several Federal penitentiaries…Today it would not be possible to recruit volunteers for such research but," Knight claimed, "the prisoners loved it." They far preferred to be in a hospital with free cokes, good food and a bit of good time pay.[19] Although Knight recalled that some abused the privilege—one prisoner escaped and robbed the Bank of Bethesda—he and his colleagues generally regarded the Prisoner Program as a great success.[20]

Launched in late 1959, the successful implementation of the Prisoner Program was largely attributed to NIH Clinical Center Deputy Director Clifton K. Himmelsbach, who had gained his experience with clinical research at the United States Public Health Service Narcotics Hospital in Lexington, Kentucky, and in two other research sites focused on research on drug addiction and narcotics prior to the opening of that facility in 1935.[21] A substantial portion of his legacy involved starting NIH's in-house prisoner program, which was designed to funnel healthy federal prisoner "volunteers" to the Clinical Center for NIAID's intentional infection research (Fig. 2).[22]

Healthy human subjects were a crucial resource for clinical research. In 1953 the NIH Clinical Center's Normal Volunteer Patient Program began with Religious Objectors, young men from Historic Peace Churches drafted for the Korean War who sought non-combat military assignment to fulfill their national service obligation. The following year NIH recruited civilians—young missionaries from institutions with which NIH contracted to provide "normals."[23] In 1959 the turn to prisoners as a population of normal subjects was neither unusual nor particularly convenient as they had to be transported from penitentiaries elsewhere. Prior to the 1970s US clinical researchers commonly used healthy human subjects who were, to use Moreno's phrase the "captive and convenient" inhabitants of total institutions on which they depended for food, shelter, and more.[24]

Several factors precipitated the NIH program through which federal prisoners were bussed or flown in to Bethesda. Some accounts suggest that there was a scientific rationale for the Prisoner Program: scientists needed batches of 25 people who entered together (rather than individuals from multiple sites with staggered arrivals) in order to ensure that immune status was shared to

[12] Latour (2000).
[13] Kutcher (2009), pp. 203–205.
[14] Aronowitz (2014); Campbell (2007); Comfort (2009) and Harkness (2003).
[15] Roth (2012).
[16] The virus we discuss here is different from the Rous Sarcoma Virus (also abbreviated RSV) that is discussed elsewhere in this issue.
[17] US Congress. Hearings on the Consumer Protection Acts (1972).
[18] Morris et al. (1956).
[19] Knight (n.d.).
[20] E.g., see oral history Wyndham Miles with C. Himmelsbach (May 4, 1972); Knight (1964).
[21] Acker (2002) and Campbell (2007).
[22] Stark (2012).
[23] Stark (2012).
[24] Goffman (2007) and Moreno (2005).

Fig. 2. The caption reads: "1964–5: Mr. Grey, Assistant Chief, NVP (Normal Volunteer Program) poses for picture depicting diet for Fed Prisoners Vols, NIAID cold virus studies".
Source: Patient Recruitment and Public Liaison Office, NIH. Image ID: b8693_4.tif.

the greatest extent possible. Institutionally isolating groups of prisoners for three to five weeks further guaranteed that they were similarly situated immunologically. By 1964, the program had brought in more than a thousand prisoners to the NIH Clinical Center, where it persisted through the end of the decade. Prisoners were used *exclusively* for intentional infection studies. By contrast healthy civilians served in investigational drug studies for cardiac conditions and psychiatric conditions, as well as other compounds, devices, and procedures then under development; and in low-hazard viral intentional infection experiments.

The Prisoner Program began in early 1960, when the first prisoners were moved into a ward prepared especially for them on the eleventh floor of the Clinical Center. A team of custodial officers was assigned to "oversee" prisoner volunteers.[25] Completing their Annual Report for that year, NIAID leaders recognized Himmelsbach's "unstinting assistance" to researchers conducting clinical investigations in the NIAID's intramural Laboratory of Infectious Diseases (LID).[26] They attributed rapid advancement in the area of viral vaccines to the Prisoner Program: "Of greatest significance for present and future programs has been the increased utilization of prisoner volunteers for clinical studies, through cooperation with the Federal Bureau of Prisons." They described the activities of a year in which "volunteers have been hospitalized in the Clinical Center, exposed to specific respiratory viruses, observed for clinical manifestations, and examined by precise laboratory techniques for evidence of infection." Prisoners were essential: "In a short time, these human volunteer studies have made available a vastly greater amount of detailed information concerning RSV and the Eaton agent than would have been possible by the usual clinical and epidemiological observations in the general population."[27]

Institutionalized populations were typically used in research on the common cold. In contrast to the derring-do of prisoner escapes or the national drama of malaria research, studies on respiratory viruses might seem less amenable to the tales of heroism that characterized research on acute or excruciating diseases such as cancer, malaria, and polio.[28] Morris and contemporaries were concerned with diarrhea and vomit, dedicating their careers to sneezes and sniffles and to working towards a vaccine against the common cold.[29] Still, respiratory viruses were pernicious and pervasive. They occasionally killed and regularly debilitated citizens and—of great concern for the US government—the corps of people responsible for the confined spaces of institutions in which the government put them: military bases, federal prisons, orphanages, institutions for the disabled, and public schools. NIH researchers collected samples from institutional sites proximate to the Clinical Center, such as a District of Columbia nursery for homeless infants named Junior Village. From the mid-1950s until the late 1960s, NIH scientists got biological samples via weekly throat swabs used to isolate respiratory viruses.[30] The longitudinal Junior Village sampling program, initiated by Robert A. Huebner and Joseph A. Bell, ended in 1969.

Junior Village studies were the direct prelude to the intentional infection studies undertaken in adult male prisoners as the viruses that Morris used were prepared from RSV samples obtained at Junior Village. Scientists isolated nearly 1,000 viruses from Junior Village children and infants as part of a collaborative NIH project titled "Epidemiologic Studies of Illnesses and Microbial Experience of Junior Village Nursery Children" (1960). After cultivating "pure" microbial cultures, scientists developed and administered vaccines to determine their effectiveness when later viral illnesses occurred in an observable "population group suitable for epidemiologic study of occurrence of infection and disease … as they occur naturally … and as they can be altered by chemo prophylaxis."[31] Like most institutions, Junior Village witnessed periodic outbreaks of para-influenza, RSV-caused pneumonia, and respiratory illnesses caused by adenovirus and associated viruses, all of which provided opportunities for study by NIH virologists. By 1967, adenovirus-associated viruses (AAV) were demonstrated to be DNA viruses requiring an unrelated or "helper" virus, adenovirus, in order to replicate. At the time of Morris' RSV study on federal prisoners, their natural history remained unknown and AAV were described simply as "contaminants of laboratory stocks of human and simian adenoviruses."[32] AAV antibodies and sero-conversions had been found in both simians and humans. NIH researchers considered the children and infants of Junior Village to offer an

[25] Like "volunteers" from other sources, prisoners were similarly referred to as "volunteers" at the NIH Clinical Center: Campbell (2007) and Stark (2012).

[26] The Annual Report also credited prison officials James V. Bennett, Director of the Bureau of Prisons, and Dr. Harold Janney, Chief Physician of the Bureau of Prisons, for their "permission and considerable assistance" with the Prisoner Program.

[27] The full text of the 1960 Annual Report may be found here: http://archive.org/stream/reportofprograma1960na/reportofprograma1960na_djvu.txt.

[28] Lederer (1997).

[29] Huebner (2005).

[30] Overall methods are described in detail in the published version of the 1960 annual report by Bell et al. (1961). Samples were collected for gastrointestinal and respiratory viruses (e.g., in the case of stomach viruses, stool samples were collected whereas in the case of respiratory viruses, throat swabs were used). The 1960 Annual Report described the Junior Village project as follows: "The study children are located in Southwest Washington, D. C. The daily population is now close to 130 white and negro babies six to ten months of age who are in residence in Eisenhower Cottage and the Infirmary for domiciliary care. The mean duration of residence is approximately 17 weeks per child. Children with illnesses are studied either in their domicile or the infirmary at Junior Village, or the Clinical Center at N. I. H., or at the DC General Hospital, depending upon the severity of illness and study interest" (p. 90).

[31] Annual Report (1960), p. 90. For example, see Kapikian, Mitchell, Chanock, Shvedoff, and Stewart (1968), at http://aje.oxfordjournals.org/content/89/4/405.abstract).

[32] Blacklow, Hoggan, and Rowe (1967).

"optimal opportunity for the isolation and characterization of AAV strains of known human origin." Junior Village research focused on viral and parasitic infections that "commonly cause misery and absenteeism from schools and industry."[33] Researchers did not induce infection; they collected virus in order to develop vaccines to respond to later illnesses "naturally" occurring in this confined institutional population.

Situated at the confluence between two streams of research, Morris became inadvertently interested in SV40 while studying respiratory viruses rather than cancer-causing viruses. Other LID researchers undertook extensive study of the natural history of cancer viruses such as mouse polyomavirus and other animal tumor viruses. In the 1959 NIAID Annual Report of Program Activities, virtually all mouse tumor virus study systems were lamented to contain extrinsic viruses, which, the report reasoned, persisted in "latent" form in tumors but might also be "tumorigenic agents" (1959, p. 10). These "fellow travelers," as they were characterized in the 1959 Annual Report, frustrated researchers seeking to understand "'models' of what (it is hoped) happens in nature" (1959, p. 11). Although the biological significance of these "extrinsic" viruses was destined to remain "obscure," there was rising interest in the "possibility that cancer could be the result of a zoonotic infection," which no longer appeared "so very unlikely" in 1960 as it had previously.[34] While skepticism that animal viruses could cause human cancers had been overcome in some quarters, practical, technical, and ideational barriers remained. By 1960 LID researchers recognized that most animal tumor virus systems were "contaminated with extraneous agents" that they believed had to be controlled if virology was to be pursued on cancer viruses. Extraneous agents were not considered a problem for study of acute viruses, but for slow-growing, often subclinical viruses that posed serious problems of detection and represented forms of "contamination" requiring systematic clean-up.

LID's viral housekeeping strategy was to establish "relatively clean," "virus defined" colonies. Realizing that "all cancer virus passage materials [that] passed through experimental animals either are known or suspected to contain extraneous viruses," scientists adopted the goal of "'clean' animals in 'clean' areas [to] finally achieve the goal of 'pure culture'."[35] While this goal might "appear monumental to some, insuperable to others, and to still others too expensive … it is also clear that reluctance to meet this problem squarely and failure to eventually achieve its solution is to accept pre-Pasteurian concepts as guides for modern virology, to waste uncounted dollars and to accept in the beginning of new and very expensive enterprises on animal tumor viruses the probability of final failure."[36] Cleanliness was considered not only an NIH responsibility, but also a hallmark of modern (post-Pasteurian) science.

Another component of modern clinical research was the review process to which Morris' section of the proposed four-part RSV study was subjected on February 9, 1960. His section fared better than others during the Medical Board's review, which did not approve other parts of the study. Comprised of NIH's head scientist-administrators, the committee was tasked with approving all studies on healthy people conducted by NIH scientists at their research hospital, as well as studies on sick people that scientists considered unusually hazardous.[37] NIH had created the committee in 1953 when the Clinical Center opened, for the express purpose of reviewing clinical research proposals that scientists in Bethesda wanted to undertake. The Committee had the power to certify (or de-certify) a proposed study. Functioning in absence of government regulations on the use of healthy people in medical research, committee decisions were regarded in quasi-legal terms aimed partly to create legal evidence in the event of a lawsuit. In short, the Committee's task was to produce clean, ethical, and legal research on human subjects by declaring clinicians' procedures acceptable or by reworking them to police contaminants that threatened to profane its product.

Committee members gave a routine endorsement to the first three respiratory viruses that Morris and colleagues proposed to study: "The Board concurred with the recommendation of the Clinical Research Committee and by unanimous vote recommended that the first three parts of the project be approved by the Director, NIH."[38] However, they had misgivings about the fourth part of the study. "It was felt that more information was needed on the PAP virus (Eaton) before final consideration of the administration of this agent into man," the Committee reported. "Upon receipt of such information the Clinical Research Committee will make recommendations to the Medical Board regarding this part of the project."[39] "Eaton agent" was later found to be a very small bacterium (smaller than some viruses and one of the smallest organisms capable of self-replication). Likely the Board was concerned that illness resulting from Eaton agent might not be treatable. There was no further consideration of the population to be involved in the study.

Each part of Morris' study, including the unapproved Eaton protocol, required that his team produce respiratory illness in human beings. Nearly a century after the legend of Robert Koch, Morris was living out Koch's postulates.[40] He sought to show that a particular agent caused a specific disease by isolating the agent; giving it to healthy people to see if it produced the expected illness; collecting samples of blood, stool, saliva, or other excretions in which to detect virus or antibodies; and again isolating the agent, thus demonstrating that it had caused the infection. Ideally, Morris would have enacted the steps recalled by Dr. Robert Couch, who was a specialist in respiratory infection and contemporary of Morris at NIAID. Like Vernon Knight, Couch arrived at the Clinical Center in 1959 from Vanderbilt. In an interview in 2013, Couch explained that "the idea of the volunteers is part of our scientific thinking, and still is. For certain things, an important approach is to prove the cause of a disease." Harkening back to his time at NIAID, he described the ideal procedure in the 1960s and the place of human subjects in that procedure:

> "It's called Koch's Postulates. And it has four components. One is that you isolate it [disease agent] from a particular disease so a pattern can be established. [For example, something] that you might see at a children's hospital or at marine base, [researchers can establish] whether it is common cold or pneumonia or bronchitis. And you take it and you give it to an animal or in this case there were basically no known animals for any of these [agents]. Maybe the language is not right. But in this case the human animal was the only potential subject … So you give the agent to the human animal. That person gets the same infection or disease or a comparable disease, and you isolate the agent back out. And those are Koch's postulates. And that's considered how you prove that agent was the cause of the original

[33] Annual Report (1960), p. 90.
[34] Annual Report (1960), p. 23.
[35] Annual Report (1960), p. 26. See also Kirk (2012).
[36] Annual Report (1960), p. 26.
[37] Stark (2012), pp. 81–111.
[38] Archives of the NIH Medical Board, Office of NIH History, Bethesda, MD (hereafter Med Board), Minutes dated Feb 9 1960.
[39] Med Board, Feb 9 1960.
[40] Geison (1995) and Latour (1993).

> respiratory disease, because of that reproduction capability. And so the need for normal volunteers for being able to do that, as all these new viruses that were emerging, was pretty clear to the people that were doing it."[41]

By rejecting Morris' proposed Eaton virus protocol, the Committee showed that it regarded some intentional infection experiments as inappropriate even for federal prisoners, who were at the time considered to be uniquely suited—morally, physically, institutionally—for other intentional infection experiments at the Clinical Center and who were brought to the Center for that purpose. By allowing the other experiments to proceed, the Committee demonstrated its eagerness to integrate the Prisoner Program into everyday experimentation at the Clinical Center.

3.2. Summer 1960: finding a stowaway, SV40

By June of 1960, Morris had his RSV study underway. Thirty-five prisoner volunteers were housed three to a room and were isolated for a few days before inoculation and for two weeks afterwards. During inoculation, Morris and his staff had subjects lie back so virus could be put in their noses and mouths, following which "the nose was massaged between thumb and forefinger by the volunteer."[42]

It was rare for studies to be reconsidered by the Clinical Research Committee, but the Committee discussed Morris' study not once, but twice. The first occasion when the study attracted the attention of the Clinical Research Committee, it considered ending it early due to concerns not about the prisoners' health, but about the health of sick children who had been brought to the research hospital for study. NIH sponsored research on RSV precisely because it caused a common, easily spread and mildly debilitating respiratory illness. However, some people, especially children, could become very sick from RSV if their immune systems were compromised. Inside the pediatric wards of the Clinical Center, researchers found their child-patients deteriorating, despite their best efforts to treat, study and care for them, because the sick children were also getting ill from RSV. Scientists traced the respiratory virus from the pediatric wards, through the hospital ventilation system, to ducts on the eleventh floor, and into prisoners that Morris and his team had infected with RSV.

As a result, the Clinical Research Committee reconsidered their approval of Morris' piece of the NIAID study on June 14, 1960. After reminding the CRC that the body had approved the study the previous February, the Committee chairman introduced Dr. Knight, who presented "some materials with reference to the utilization of Respiratory Syncytial Virus in which," the chairman said, "there has been recently noted the appearance of pneumonitis in children in which this virus was implicated." Morris' virus was emblematic of a systemic problem: human subjects—sick and well—were being compromised both as patients and as "research material" when they became ill from other diseases. Most of these extraneous illnesses were from cross-contamination. Of 70 cases recorded in one period, 46 cases were "cross infections."

The Committee ultimately decided to let the study continue, which illustrates the high level of discretion and trust accorded to investigators by the NIH's leading scientist-administrators—men who were their peers operating in a system reminiscent of arrangements of gentlemanly decorum. The Committee's meeting minutes record that "[a]t the close of the discussion, the members of the Clinical Research Committee and the Medical Board, relying on the good judgment of Dr. Knight and his colleagues and their advice to the Committee that this is a relatively minor illness, recommended that the approval of this project be continued."[43] Knight and his peers on the committee reconciled their working ethic with NIH's justification for sponsoring the study in the first place. Once underway, NIH studies were rarely discussed; investigators worked with a paradoxical sense of autonomy. As much as NIH leaders appeared genuinely to believe that government scientists were doing independent research on the cutting edge of science, they also worked to create an image of oversight in which predictable hazards were contained and routines of cleanliness, protection, and safety carefully carried out.[44]

Thus it was all the more unusual that Morris' RSV study drew the NIH CRC spotlight a second time in June of 1960. This time it was due to an extraordinary announcement from Maurice Hilleman, director of vaccine research at the Merck Institute for Therapeutic Research in West Point, Pennsylvania.[45] On Monday, June 3, 1960, Hilleman had spoken on the topic of "detection of non-detectable viruses" at the Pan American Health Organization meetings in Washington.[46] Not surprisingly given Merck's role in producing Sabin vaccine, Hilleman had become concerned about the presence of previously non-detectable simian viruses in the kidney cell stocks used to produce the live-virus vaccine and asked senior research scientist Benjamin Sweet to investigate. The team detected 40 simian viruses. Hilleman was especially concerned with the fortieth, which had been dubbed "vacuolating virus" and was known to damage animal and human tissue cells.[47] NIH DBS scientists Bernice Eddy and Sarah Stewart had published a series of at least nine studies between 1958 and 1960 showing that "vacuolating virus" induced tumors in mice and hamsters.[48] Hence when Hilleman announced that a previously "hypothetical 'non-detectable' simian virus"[49] had not only been detected but shown to cause cytopathic changes in cell cultures, the stowaway was named and conscripted into the political and scientific conflict over the polio vaccine, which pitted the Sabin oral live vaccine against the Salk injected killed polio vaccine. Hilleman and Sweet showed that SV40 was present in pooled rhesus monkey kidney cells used to prepare and test polio and adenovirus vaccines.

Although SV40 was later shown to have been present in both Sabin and Salk polio vaccines,[50] it was possible to think in 1960 that

[41] Oral history interview, Laura Stark with Dr. Robert Couch, May 1, 2013, Nashville, TN. Archive: Science and the Subject's Perspective. Quotation location 20:20.

[42] Morris et al. (1961), p. 65. Morris also wrote on page 58, "Our interest in SV40 is centered around Sabin [who] has reported evidence which leads him to conclude that SV40 when administered orally fails to infect man." This paper also notes that, "Our studies on materials made available to us by Dr. Sabin support his idea. These materials consisted of a sample of type 1, live, attenuated, oral polio vaccine strain LSC, which had been administered to 12 children whose paired sera were also submitted to us for examination in SV40 neutralizing antibody tests."

[43] Med Board. June 14, 1960.

[44] Kutcher (2009).

[45] On Merck, Sharpe & Dohme's role in the postwar research apparatus, see Tobbell (2011).

[46] Sweet and Hilleman's preliminary findings were presented at the June 1960 meeting of the Second International Live Poliomyelitis Vaccine Conference, sponsored by the Sister Elizabeth Kenny Foundation, at the Pan American Health Organization headquartered in Washington, D.C. and held at Georgetown University. In their presentation, titled "Detection of a 'non-detectable' simian virus," Sweet and Hilleman reported finding the SV40 virus, a hitherto unknown agent. On the Kenny Foundation's role in funding polio research and treatment, see Rogers (2013) and International Conference on Live Poliovirus Vaccines (1960).

[47] Sweet & Hilleman (1960). The original paper and subsequent discussion is in PAHO (1960). The episode is also described in Bookchin & Schumacher (2005), pp. 71–76.

[48] Bookchin & Schumacher (2005), pp. 57–68. See also Eddy & Stewart (1959).

[49] Sweet and Hilleman (1960); also described in Bookchin & Schumacher (2005), p. 74.

[50] Cutrone, et al. (2005) and Sabin & Boulger (1973).

live virus vaccines could be purified of simian viruses. This was indeed what Hilleman recommended since data on short-term effects were "either meager or entirely lacking," and he considered his findings "scanty and still in progress."[51] Nevertheless the tenor of his remarks led top scientists at the meeting to conclude that "one cannot assume that these viruses are harmless."[52] Following Hilleman's presentation, one scientist summed up: "Until today we were not aware of this agent. It is possible we did not recognize its effects in the cultures, but of course its effect would be masked by the destruction of the cells resulting from the poliovirus infection."[53]

Once SV40 was sighted, a new past in which the SV40 virus—and possibly other wild viruses—were always already present in monkey cell cultures that were used in the production of vaccines came into being. What did this revelation mean? Hilleman later disclosed in a widely circulated interview with historian Edward Shorter that he not only suspected that SV40 was different than other simian viruses but told Sabin that this one might cause cancer.[54] By 1960, it is estimated that 98 million people had received contaminated polio vaccines prepared with rhesus monkey kidney tissue, so Hilleman's announcement at the Pan American Health conference caused serious concern in Bethesda. The NIH's Division of Biological Standards was solely responsible for testing batches of vaccine to ensure that manufacturers met quality control standards. Thus NIH was concerned about the implications of SV40 for research, about the scope of DBS responsibility, and about the extent of NIH liability.[55]

Potential SV40 contamination was a problem because both research and vaccine production relied on monkey kidney substrate. This was quite clear to Morris. His RSV samples were prepared using rhesus monkey kidney tissue, which was the standard preparation for all researchers studying adenoviruses (including RSV) and also for mass production of millions of live and killed polio vaccines that had been administered in the USA and around the world since 1955. Following Hilleman's visit, Morris wondered whether his material was contaminated with SV40. Indeed, when tested as the RSV experiment was in progress, Morris found that the RSV pool he had given to prisoners for experimental infection was contaminated with SV40.[56] Although it can be difficult to gauge the emotional intensity of such a finding at the time, the scientific literature—a genre not known for exuberant conventions of expressiveness—suggests that anxiety was high within NIAID once researchers were certain of SV40 contamination. Animal research and eventually human tissue studies showed that the "vacuolating virus" produced tumors under some conditions. Moreover, the use of formalin, which was previously assumed to neutralize the virus, had not impeded tumor formation.[57] Forced to end the experiment early, Morris was unsure what SV40 did to people. But NIH clinicians knew that it had caused cancer in hamsters,[58] and two dozen scientists at NIAID (including Knight and Morris), knew that SV40 had been given to human subjects. NIH administrators also knew they had approved millions of batches of polio vaccine prepared with the rhesus monkey tissue that had recently been found to contain an unidentified contaminant, which they now suspected to be SV40 stowing away.

The unexpected appearance of SV40 in Morris' RSV study represented both crisis and opportunity. At that time, science-administrators were grappling simultaneously with evidence suggesting that animal viruses could cause human cancers, and the logistical realities of starting up a new channel for transporting federal prisoners to the research hospital located on the main NIH campus. For the NIH Clinical Center, the implications of cross-species transmission of disease were wide ranging. First, cross-species transmission meant there were new potential disease outbreaks that would affect the American population: sicknesses from birds, cows, and pigs.[59] Second, cross-species transmission meant that laboratory workers could become ill from laboring with and around animals, barnyard animals, urban-dwellers, and exotics alike. The first clear-cut evidence of cross-species transmission of simian malaria had led to the deaths of two NIH investigators that year, in response to which the NIH Clinical Center changed its research program.[60] Third and most important, vaccines were prepared on animal tissue substrates in the days before the distribution of the HeLa cell line. Evidence of cross-species transmission made it now imaginable that vaccines so prepared could sicken people with diseases unrelated to the one for which the vaccine was designed. Consider the possibilities in 1960 for NIH scientists researching both simian and human malaria strains, who were conducting intentional infection experiments at the Clinical Center. Animal tissue was also used to develop vaccines against influenza viruses and the so-called common cold. In sum, the new conceptual world of the early 1960s in which viruses could cross species lines reshaped biomedical knowledge, practice, and production.

To be sure, cross-species transmission had implications beyond NIH walls for reshaping cross-species interactions. Humans and nonhumans alike became social actors in laboratories of a different sort than existed prior to this moment: animal viruses became potentially dangerous to humans at a time when tools and techniques for studying the effects of animal viruses on humans had been only recently developed. Researchers developed new channels for the importation of monkeys in an attempt to bring virus-free animals into their laboratories. Hilleman shifted to African green monkeys imported via Philadelphia to avoid the rhesus macaques imported through New York for malaria research and vaccine research and preparation.[61] By mid-1960 Hilleman had identified dozens of viruses indigenous to monkeys present in both live and killed polio vaccines.[62] This co-presence of many wild viruses was obscured by the singling-out of SV40, which was then

[51] Sweet & Hilleman (1960), p. 79.

[52] PAHO (1960), p. 86.

[53] PAHO (1960), pp. 88–89.

[54] The edited and excerpted video interview has taken on the dimensions of a cultural phenomenon known as the "zombie meme."

[55] Responsibility for regulating vaccines moved to the Food and Drug Administration in the 1970s and NIH responsibility for regulating human subjects research migrated to the newly created Office for Protection from Research Risks in the same decade. Although NIH reluctantly assumed responsibility for stem cell research in the twenty-first century, administrators have generally regarded it as a bad idea to have NIH regulate research in which its own scientist-employees participate because of their stake in research outcomes. See Marks (2011) and Offit (2005).

[56] Morris, et al. (1956).

[57] Gerber (1967) noted that "large groups of the population in this country and abroad must have been injected with varying amounts of SV40 during the course of immunization with formalinized poliomyelitisis and adenovirus vaccines," p. 90.

[58] Eddy & Stewart (1959).

[59] Slater (2009) and Mitchell (2005).

[60] In 1961, for example, NIH insisted that prisoners enrolled in simian malaria studies be moved to the Clinical Center in Bethesda only "after they had received a 'take' from the malaria," which would occur at the prisons. Med Board, Nov 28, 1961.

[61] To imagine the scale of the effect, consider that only around 100,000 monkeys and apes were imported into the USA annually by the end of the 1960s, and yet by 1967, American scientists were using monkeys and apes in nearly a thousand laboratories with a total budget of 55 million dollars. Kalter & Heberling (1971).

[62] Hilleman's concern with SV40 was a direct effect of the scaling up of vaccine manufacture using pooled monkey kidney substrate. The risk of SV40 being present in any given individual rhesus monkey was low; only when large numbers of animals were shipped and caged together and their cells pooled did risk of viral transmission increase. U. S. Department of Health and Human Services, 1997, Hilleman remarks, pp. 260–262.

dismissed to render it insignificant to the American public, if not to NIH scientists and administrators.

In the context of new studies of cross-species transmission, SV40 reoriented the material conditions and social relations of the NIH Clinical Center in the early 1960s as NIH virologists searched for ways to reconcile dissonance between standards, ideals, and everyday practices of clinical research. While virologists adhered to Koch's postulates, they knew that animals were poor models for identifying viruses that caused human illness because they were also reservoirs of viruses that could potentially affect people. It went almost without saying that studies would have to be done on intentionally infected humans. Yet scientists recognized moral conventions that channeled their actions and research practices—the things they were willing to do or not do—without systematically and routinely creating the paper trails that became common after the mid-1960s.[63] Their commitments were tacit rather than codified, practical rather than formal. To be sure, the lexical content of scientists' moral and ethical commitments differed from those that would be written down and enforced (and eventually embodied and enacted). Still informal, little-documented standards permeated local research settings such that it cannot be argued that there were no ethical norms in play.[64] Regarding cancer-virus research in particular, virologist Albert Sabin argued against clinical cancer-virus research on grounds that it was "ethically impossible" to infect and then re-infect human subjects with a known cancer-causing agent.[65] Others at NIH, such as scientist Robert Couch, recalled the impact of the simian virus revelation in the summer of 1960:

> "Simian Virus 40 was a contaminant of the rhesus monkey kidney tissue cultures that had been used for making some of the earlier vaccines, including the Sabin vaccine, the live vaccine as well killed, which actually was a little bit more concerning than the Salk vaccine because the Salk vaccine, when it was done up, you killed everything with formaldehyde and so that should have killed SV40."

Reflecting on NIAID in the early 1960s, Robert Couch asked himself, "Would that contaminant be studied in normal volunteers?" His answer: "Absolutely not. It would never be considered because it was considered to be a potential tumor producer. I never even heard that as an option discussed but it would have been rejected by the scientists, not to mention review committees. [44:15]"

Couch believed in retrospect that there was no possibility that clinical research on SV40 would have been done. Yet in 1960 Morris did indeed conduct a second study on the very prisoners who had been contaminated.[66]

"Our interest in SV40," Morris and coauthors wrote, "is centered around its potentialities as an infectious agent in man."[67] Setting out to re-isolate SV40 from the bodily fluids of prisoners used in the RSV study and to understand the clinical effects of SV40, Morris sought to answer these questions for two different cases in which prisoners got RSV and SV40 together. In the first instance, he gave prisoners one inoculum containing both RSV and SV40. Morris used 16 prisoners for this arm, half of whom also got an antibody for SV40, and half of whom also got an antibody for RSV. In the second instance, he gave prisoners an inoculum of SV40 and, separately, an inoculum of RSV and an SV40 antiserum. To serve as controls for the entire study, three prisoners got a placebo inoculum—no SV40 or RSV.

When his results were published a year later, Morris reported that his team had re-isolated SV40, which meant that the polio vaccine was infected with a tumor-causing agent. He reported that his team also found that SV40 caused a mild subclinical infection. His results became an essential citation for scientists aiming to understand SV40's role in human disease. Within two years of Morris' clinical study, microbiologists at NIH had produced evidence that SV40 caused cancer in animals. Epidemiologists have since been unable to show a relative increase in cancer in the millions of children who received SV40 with their polio vaccines.[68] The Sabin oral live polio vaccine was later shown to contain high-titer SV40 detectable in the human gut, but appeared to cause no systemic infection.[69] Recipients of the Salk attenuated polio vaccine received lower dose SV40 but did form detectable antibodies.

The equivocal nature of SV40's effects became part of its characterization, which persists into the present. For instance, Arthur Levine opened the second day of the U.S. Department of Health and Human Services 1997 workshop with the summary of the previous day's testimony: "First, SV40, at least in the form of its DNA, is or is not present in human tumors, and is or is not present in normal human tissues. And, we heard compelling data on both sides of that question, all from good labs, and I think that the question will only be resolved by an appropriately blinded study." Technical matters such as dosage (high titer or low titer); the relative efficacy of formalin used to cleanse vaccines of SV40; and the sensitivity of the PCR technique entered into Levine's question, "Is this an agent that we live with, and that we've always lived with, independent of the poliovirus vaccine exposure?" This is another way of characterizing SV40—as a human commensal. There is even some evidence that SV40 may be involved in suppressing tumor formation and thus may have cancer-fighting properties. We do not seek to come to a conclusion about the scientific evidence so much as to illuminate the forms of practical reasoning with which the scientific community has historically approached SV40.

While it is possible to see Couch's recollection and Morris' subsequent decision to give prisoners SV40 as contradictory, we see it as evidence of NIH scientists' practical reasoning regarding contamination circa 1960. A feature of this practical logic was a particular understanding of the existence of the virus as predating its moment of human discovery.

The fact that the prisoners were now known to be exposed to SV40 constituted them as a new research population. Scientists' ontological world was different at the end of June than it had been at the beginning of that month. At the end of June, scientists' identification of SV40 in an unexpected context—which is to say, as a stowaway in cultures at the NIH Clinical Center—changed not only contemporary science, but also scientists' understandings of the past. As a result, the prisoners who had already been unwittingly subject to the risk of SV40 were the *only* viable, ethical, and scientifically sound human population in which to research it. The exposure constituted a new research population and the definition

[63] Himmelsbach and the Bureau of Prisons required written consent-liability release forms from prisoners, but scientists resisted a blanket policy to require all healthy human subjects to sign consent-release forms until 1963. Himmelsbach, on the other hand, had a working knowledge of the need for informed consent as early as the mid-1930s. See Campbell (2007), Stark (2012: 113–135), and Slater & Humphreys (2008).

[64] Halpern (2006).

[65] Subcommittee on Government Research, Research in the Service of Man: Biomedical Knowledge, Development, and Use, S. Doc. No. 90-55, at 163 (1966) (Conference Rep.).

[66] The study took place at the NIH Clinical Center. NIAID's prisoner ward held at most 27 prisoners. Morris' study enrolled 46 subjects, so he had to have used prisoners from at least two different "deliveries." He learned of SV40 in mid-June and reported his findings at NIH in August. Prisoners were enrolled in the study for 3 weeks. It seems likely that those originally enrolled in the RSV study were used again in the SV40 study. It was common to use prisoners in more than one study during their stay.

[67] Morris et al. (1961), p. 58.

[68] Results from Shah & Nathanson (1976) showed no relative increase in cancer.

[69] U. S. Department of Health and Human Services (1997), p. 264.

of SV40 allowed them, with haste, to undertake a study that would enable SV40 to take on more precise attributes.

3.3. Fall 1960: giving meaning to SV40

Morris' findings from the clinical study of SV40 anchored NIH leaders' claim that the virus was an irrelevant, if unexpected, addition to cultures and sera widely used in research and vaccine production from the 1950s through the early 1960s, including his own previous research on RSV. As a result, by the end of 1960, NIH leaders began to reason that SV40's presence, which was presumed to have widely contaminated trials and therapies during the previous decade, neither invalidated prior research nor jeopardized human health in the large-scale vaccine programs. Thus, SV40 played a formative role at the NIH Clinical Center in shaping local conventions of judgment, shared beliefs, and, eventually, notions of ethical research—which continued to influenced national debate in the ensuing decades.

In September of 1960, the CRC approved the fourth, previously unapproved, part of the NIAID respiratory infection study, which examined Eaton virus. When CRC members reconsidered the protocol, however, they also added a component for the study of SV40 to be conducted on prisoners: namely, Morris' summer study. Contrary to contemporary scientists' expectations, such as those of Dr. Robert Couch quoted in the previous section, the NIH CRC approved Morris' clinical research on SV40, which by definition made it legal and ethical (by local, contemporary standards) to proceed with the research. Morris had presented his summer findings at a Clinical Center staff meeting in August. Then on September 6, 1960 CRC members approved the Eaton protocol that they had not approved in February, which now included an additional protocol to follow up on SV40. Medical Board meeting minutes show that the clinical leaders officially approved the study called "Use of Human Volunteers in Experiments with Eaton Virus (Primary Atypical Pneumonia Virus) and Simian Virus—Research Procedure of NIAID."[70] NIH Director James Shannon followed suit and approved the study when it came across his desk. It is worth noting that in the same meeting, NIH leaders agreed to send a letter to NIH's contact at the of US Bureau of Prisons, Dr. Harold Janney, "expressing the Board's appreciation for his cooperation in the recruitment of normal volunteers from the Federal prison system for certain of our research studies."[71] This new channel for getting human research materials in the Clinical Center appeared to be working well despite the disruption occasioned by the appearance of SV40.

While late 1960 might appear uneventful in retrospect, this appearance was the outcome of craft. In their year-end account, leaders of NIAID described 1960 as a productive year for the NIAID. The 1960 Annual Report dwelt upon the problem posed by extraneous viruses that were cast as "background noise," managing potential concerns about SV40's negative impact by emphasizing that work on respiratory viruses was entwined with emerging interest in cancer viruses.[72]

The Annual Report noted that in the year 1960, the problem of contamination had grown beyond "background noise" to constitute a problem of "'deafening' proportions" that was the biggest obstacle to "intelligent and truly effective research on cancer viruses. Nearly every animal tumor virus system currently under study was shown to be contaminated with extraneous agents and several viruses widely proclaimed as 'tumor' viruses turned out to be 'fellow traveling ordinary viruses'."[73]

Thus by 1960 virologists within NIAID (specifically, the Laboratory of Infectious Diseases) viewed animal viruses either as "extraneous" or as "fellow traveling ordinary viruses." They understood the sudden appearance of such viruses as produced by recent technological innovations enabling these agents to show up where they had not shown up before. This new concern was layered upon LID's ongoing work with the vast collection of respiratory viruses gathered from institutionalized children, including those at Junior Village, in the 1950s. When in 1960 clinical study of acute respiratory infections with a few of these viral agents got underway, the additional investments required to initiate the Prisoner Program were seen as worth the effort to produce a "rather uniform 'cold'." Both RSV and the prison population were viewed as ways to standardize research with respect to immunity and enable a dose-response metric in which the "subsequent rise in complement-fixing antibody appears to correlate with severity of illness."[74] Although the Annual Report had little to say about SV40, it went into detail about the discovery that simian malaria could infect human beings that had been occasioned by several accidental infections of laboratory workers from monkey bites. From the point of view of the official report to Congress, then, the discovery of SV40 seems to have been regarded as far less of an alarming event than it initially appeared.

By year's end, NIH scientists had decided that SV40 did not threaten human health. Yet this issue has defied closure in the longer term. Questions about long-term effects of SV40 are today almost as unsettled as when they first appeared on the ethical and scientific horizon in the early 1960s.[75] SV40 acquired multiple meanings ranging from benign background to a possible cancer *suppressor* with therapeutic uses,[76] to an "emergent threat," a killer stalking vulnerable children whose parents followed a prescribed vaccination schedule.[77]

SV40 has continued to reappear in unexpected places and moments. Today SV40 is understood to be a model system for studying viral pathogenesis, cell transformation and growth, eukaryotic gene expression, and DNA replication.[78] SV40 sequences have been found in people too young to have received polio vaccine containing it, and in a variety of cancers throughout the world. SV40 figures

[70] Med Board. 6 Sept 1960.

[71] Med Board. 27 Sept 1960.

[72] The report described the links between research on cancer and on viruses: "(a) Laboratory studies of the properties of cancer viruses and development of laboratory tools for detecting and working with them; (b) Field studies of the behavior in nature of those tumor viruses for which suitable detection tests are available; (c) Studies of extraneous viruses ('background noise') now preventing high caliber virologic practice in the study of animal tumor viruses and obscuring interpretation of nearly all current observations on them; and (d) The study of general virus experiences in relation to human cancer—the 'background noise' in the human cancer problem—which must be done eventually if the role of viruses in human cancer is to be defined." Annual Report (1960), p. 31.

[73] Annual Report (1960), p. 32.

[74] Annual Report (1960), p. 32.

[75] Schmeck, Jr. (1981). A fragile scientific consensus was achieved in the early 2000s, when the National Cancer Institute published a series of studies by Engels, Viscidi et al. (2004), Engels, Chen et al. (2004), Engels, Switzer, Heneine, & Viscidi (2004) and Engels et al. (2005). Today SV40 is known to cause mild human illness and to be present to varying degrees in different human populations (Osmundsen, 1965; Vanchiere et al. 2009). However, SV40 is also represented as a potentially "emergent threat" by the Butel laboratory at Baylor University, which conducted a meta-analysis revealing "significant excess risk of SV40 associated with human primary brain cancers, malignant mesotheliomas, bone cancers, and NHL compared to control samples." Vilchez & Butel (2009) concluded that there was "mounting evidence … that SV40 is a human pathogen, and current molecular biology, pathology, and clinical data, taken together, show that SV40 is significantly associated with and may be functionally important in the development of some human malignancies." See also (Grady, 2002).

[76] SV40 viral vectors have been modified for gene delivery, including the delivery of cancer therapies. Vera & Fortes (2004).

[77] Horwin v. American Home Products, American Cyanamid Company, Lederle Laboratories, 2000.

[78] Hilleman (1998) and Javier and Butel (2008).

repeatedly as a stowaway in new historical moments and social spaces, as seen, for example, in the open-ended conclusion of the 1997 U. S. Department of Health and Human Services Workshop on SV40, which brought together the Food and Drug Administration, the Centers for Disease Control, and several NIH institutes.[79]

SV40 pervades the social worlds of pharmaceutical vaccine development; societal response to vaccines, including a parents' movement linked to HIV-AIDS activists who locate the origin of HIV in cross-species transmission; the sciences of microbiology, virology, viral oncology, and immunology; and the social organization of Big Science that is the NIH. Wherever SV40 appears unexpectedly, it pressures conceptual configurations, research practices, features of the physical environment, and ethical understandings. Yet people's causal claims about SV40 and cancer have remained unstable. This lack of closure would seem to hold potential for ethical and legal repercussions, but it has primarily enabled SV40 to catalyze innovations in virology, infectious disease and cancer research, public health epidemiology, and vaccine development from the early 1960s to the present.

The jury remains out on most aspects of SV40. An Immunization Safety Review committee convened by the Institute of Medicine (2002) recommended further biological study to resolve technical issues that would prevent further study of SV40's transmissibility between humans. At the same time, the IOM committee recommended against any more epidemiological assessment in human populations. Although SV40's biological properties were "consistent with a cancer-causing virus," the Committee found the "evidence was inadequate to accept or reject a causal relationship between SV40-containing polio vaccines and cancer."[80] No increased cancer risk was identified in numerous epidemiological studies of populations exposed to contaminated polio vaccine. Yet scientists have presented compelling evidence of SV40 DNA sequences appearing in human mesotheliomas, osteosarcomas, and a growing list of other human cancers.[81]

Technical issues have prevented scientists from uniformly documenting the presence of SV40 DNA in human cancers. In addition, three main social and organizational arrangements have continued to vex scientists. First, scientists are funded and organized to focus on oncogenes, rather than the oncoviruses that directed research on SV40 in previous decades.[82] Second, scientists lack evidence that SV40 plays a causal role in human cancer; SV40 DNA is not present in each cell of the human cancers in which it appears.[83] Third, scientists have found that SV40 has an affinity for some human tissues and not others, and some human populations and not others.[84]

Thus, in the twenty-first century, scientists started to speculate that SV40 was present in human populations even before contaminated polio vaccine was widely administered between 1955 and 1963—another version of the always-already narrative. To date, there is no SV40-specific serological assay useful in clinical populations, despite evidence that implicates the virus in human malignancies, which scientists have found compelling with the evolution of PCR techniques. Concluding that the SV40 puzzle is missing several pieces, Garcea and Imperiale (2003) muse that "perhaps we expect SV40 to follow the 'rules' for other oncogenic viruses such as human papillomavirus and Epstein–Barr virus. Rather, SV40 may be generating novel rules, leading the way as it has before into new paradigms of virus biology and pathogenesis."

In sum, the NIH built a research setting that yielded interlocking but inconclusive research agendas that explored both cancer and virus, and created a social situation in which the narrative of vaccine development could still be construed as holding SV40 at bay. The story of SV40 is the story of a stowaway that came to light and that was quickly and quietly processed into stylized mechanisms of control designed to manage SV40 through legal, scientific, technical and interpersonal means.

4. Conclusion: stowaways in history of science and philosophy of history

There has been no effort to replicate Morris' study despite scientists' continuing uncertainty about the effects of SV40 on humans, a question that has fueled policy debates, scientific controversies, and conspiracy theories over the past half century. One aim of this paper has been to explain historically why there were not multiple clinical experiments designed to settle the matter, or no clinical studies at all. Indeed, replicating the study in non-prisoners would have speeded and sealed NIH's political and practical management of SV40 and the potential crisis that it posed to biomedical research both in 1960 and in more recent decades. Alternatively, refusing to conduct any clinical study of SV40 in the first place would have avoided any appearance of unethical conduct at NIH. As we showed, two historical moments were particularly freighted. The first moment was in the summer of 1960 when Morris intentionally gave SV40 to federal prisoners after discovering that he had previously infected them during a series of studies conducted that spring. The second moment came three months later when NIH leaders approved the SV40 intentional-infection experiments that Morris had completed that summer. None considered Morris' clinical study on healthy prisoners unethical. SV40 was not the first but the fortieth simian virus detected by June 1960, and yet it was unclear if these viruses threatened human health. Ultimately, Morris reported that SV40 had negligible effects on healthy prisoners.

Using SV40 as an exemplary stowaway, we have argued that when scientists identify such a previously undetected entity, they initiate a process that redefines objects of study; reconfigures understandings of research populations, materials, and settings; and enables the appearance of new ethical and epistemic horizons. Once revealed, a stowaway such as SV40 may be rendered more or less active depending on the social, historical, and, in this case, political circumstances.

In elaborating the case of SV40, we hoped to accomplish an additional aim: to develop an analytic device from the philosophy of history, namely the stowaway. Like all contaminants, once stowaways are revealed within a specific context, it is difficult—often impossible—to make them nonexistent in social and material worlds (though see Hacking, 2004). Once stowaways have been revealed, moreover, they can travel to new locations as time passes, either with people's full awareness or again concealed. One distinctive feature of stowaways, however, is that they alter scientists' future as well as their past. The possibility that a given stowaway can turn up out of place in the future stokes continued uncertainty about when and how, precisely, stowaways get into improper places.

Stowaways make it difficult for people—scientists, staff, and policymakers—to establish certainty about the past, which is important for those who work to assign blame, assess effects, and remediate consequences. While it goes without saying that people cannot return to the past, we have argued that it is equally

[79] Levine in U.S. Department of Health and Human Services Workshop, Part II, January 28 (1997), p. 6.
[80] IOM (2002), p. 75.
[81] Garcea & Imperiale (2003).
[82] Creager (2002).
[83] Garcea & Imperiale (2003) note that this lack of association distinguishes the role of SV40 from the role of Epstein–Barr Virus in lymphoma or human papillomavirus in cervical cancer.
[84] Lapin & Chikobava (2009).

impossible for scientists to think and act in their present moment with the same version of the past once a stowaway has been revealed. In other words, it is impossible for actors to recapture in their present moment previous understandings of the past. Using the case of SV40 we further suggest that empirical evidence and ethical evaluations of stowaways are co-constitutive and thus must be produced together. In 1960 the empirical evidence that scientists needed in order to settle ethical questions about SV40 threatened to create the very ethical problem in question: the possibility of endangering human health through clinical research on SV40. Stowaways in science reveal that empirical evidence and ethical endorsement of research depend on each other. As a stowaway, SV40 has reanimated several rounds of federal hearings, popular controversies, and scientific publications in which Morris and many other researchers participated well into the 21st century. This persistent debate about SV40 continues to resound as scientists and stakeholders have used Morris' findings to manage SV40 politically and epistemologically since 1960.

Most histories of cancer research focus on the organized search for etiology and treatment.[85] By contrast histories of cancer-virus research have often been told as accounts of science left undone, in which researchers were marginalized because their frameworks and findings diverged from prevailing thought styles or paradigms.[86] Yet the history of SV40 cannot be exhausted either by Cold War frameworks applied to the War on Cancer or by the narrative of agnotology.[87] Political and epistemological debates about SV40 emerge episodically, at odds with triumphalist narratives central to stories concerning the progress of biomedical research. As a result, the history of SV40 refracts in useful ways for the history and philosophy of biology and medicine. Rather than document a search for a cause, prevention, or cure, this paper recounts the performance—the bringing into being—of a new research object and its effects not only on the future but also on contemporary and current understandings of the past.[88]

By documenting the remarkable trajectory of SV40, we have shown how this stowaway altered the social organization of knowledge in the terrain of vaccine production after 1960, affecting how scientists and science administrators; patients and human subjects; nurses, lab technicians, and research coordinators; policymakers; and historians of science, technology, and medicine could think about the past as well as the future. As the concept of the stowaway develops in the philosophy of history, we encourage scholars to explore how such refinements alter our own arguments and to insert more cases from the history of the biosciences into the philosophy of history. After all, creating history, like creating science, is a process of knowledge production open to study, reflection, and change.

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[85] E.g., Kutcher (2009); Proctor (1996) and Wailoo, Livingston, Epstein, and Aronowitz (2010).

[86] See Bookchin and Schumacher's account of the scientific work of Sarah Stewart in the National Cancer Institute and Bernice Eddy in the NIH Division of Biological Sciences on oncology and "experimental virology", pp. 60–68. Morris later became a highly politicized figure in the context of controversy over swine flu vaccines in the 1970s.

[87] Proctor & Schiebinger (2008).

[88] Performance theory is derived from J. L. Austin's philosophy of language (1975), and updated by others such as Donald MacKenzie (2009). We are not using the dramaturgical approach of Erving Goffman and others, in which "performance" resonates with theater, as in Stephen Hilgartner's use of the term.

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